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EXAMINER
WHALEY, PABLO S

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)
Office Action Summary	10/634,145	HENG ET AL.
	Examiner	Art Unit	
	Pablo Whaley	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
  Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _28 September 2007_.

2a)☐ This action is **FINAL**.   2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _1-15 and 17-30_ is/are pending in the application.

   4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _1-15 and 17-30_ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

   Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

   Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   a)☐ All b)☐ Some * c)☐ None of:

   1.☐ Certified copies of the priority documents have been received.

   2.☐ Certified copies of the priority documents have been received in Application No. _____.

   3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

   * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO/SB/08)
   Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413)
   Paper No(s)/Mail Date. _____ .

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

DETAILED ACTION

Request For Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/28/2007 has been entered.

Claims Under Examination

Claims 1-15 and 17-30 are herein under examination. Claim 16 is cancelled.

Priority

Priority to this application's U.S. filing date of 8/4/2003 has been acknowledged.

Withdrawn Rejections

The rejection of claims 1-15 and 17-30 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendments to the claims, filed 09/28/2007.

The rejection of claims 1-15 and 17-30 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicant's arguments, filed 09/28/2007.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-15 and 17-30 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter.

Claims 1-15, 17-19, 22-26, 27, and 28-30 are drawn to computer-implemented methods. Claim 20 is drawn to a system for performing the methods recited in claims 1-15 and 17-19. Claim 21 is drawn to an article of manufacture (i.e. program) for carrying out a method. For a process to be statutory, it must provide: (1) a practical application by physical transformation (i.e. reduction of an article to a different state or thing), or (2) a practical application that produces a concrete, tangible, and useful result [State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998)], [AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)]. As noted in State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), the statutory category of the claimed subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result. The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to a process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility. Therefore, for a system and program that carry out a process to be statutory they must also provide a concrete, tangible, and useful result.

In the instant case, the claimed processes do not result in a physical transformation of matter. Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible (i.e. communicated to a user), and useful result (i.e. a specific and substantial). Claims 1-15, 17-19, 22-26, 27, and 28-30 result in minimizing data to obtain optimized parameters. This is not a tangible result because this step does not communicate a result in a user readable format. Therefore the claimed method does not recite a practical application of a 35 U.S.C. 101 Judicial exception and is not statutory. By similar reasoning, the claimed program and system are not statutory for the following reasons. In the instant case, claim 20 is drawn to a system for performing the methods recited in claims 1-15 and 17-19. Because the method of claims 1-15 and 17-19 does not recite a tangible result for the reasons set forth above, the system also does not recite a tangible result. Claim 21 is drawn to an article of manufacture (i.e. program) for carrying out a method that results in minimizing data to obtain optimized parameters so that a risk is calculated. This is not a tangible result because the claim does not require the communication of a real-world (i.e. tangible) result in a user readable format. Therefore the claimed product and system do not recite a practical application of a 35 U.S.C. 101 Judicial exception and are not statutory.

This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment. For an updated discussion of statutory considerations with regard to non-functional descriptive material and computer-related inventions, see the Guidelines for Patent Eligible Subject Matter in the MPEP 2106, Section IV.

Response to Arguments

Applicant's arguments, filed 9/28/2007, that the instant claims now require the storage of data to a machine and produce a real-world result (i.e. "to predict a disease risk") and thus recite a tangible result [p.10] have been fully considered but are not persuasive. As explained above, the storage of information to a computer does not constitute a tangible result because nothing is communicated to the user in a user-readable format. Furthermore, the limitation of "to produce a disease risk" is an intended use. Therefore the claims do not require the production of a result that is indicative of the disease risk, per se.

Applicant's arguments, filed 9/28/2007, that the storage of a statistical model to a computer changes the state of at least one computing device have been fully considered but are not persuasive. The claims do not require an explicit physical transformation of a component of a computing device that is sufficient to establish that "storing" a statistical model to a computer is statutory subject matter under 35 U.S.C. 101. Furthermore, the claimed statistical model does not impart any structural and functional interrelationship between itself and the computer components such that functionality is realized. Therefore, the model is interpreted as non-functional descriptive material stored on a computing device which is not statutory subject matter (e.g. music stored on a compact disk). For the reasons set forth above, the claims are not statutory. For an updated discussion of statutory considerations with regard to non-functional descriptive material and computer-related inventions, see the MPEP Section 2106.01.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or
described as set forth in section 102 of this title, if the differences between the subject
matter sought to be patented and the prior art are such that the subject matter as a whole
would have been obvious at the time the invention was made to a person having ordinary
skill in the art to which said subject matter pertains. Patentability shall not be negatived by
the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims
under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims
was commonly owned at the time any inventions covered therein were made absent any
evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point
out the inventor and invention dates of each claim that was not commonly owned at the time
a later invention was made in order for the examiner to consider the applicability of 35
U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 3, 9, 19, 20, 21, 23, and 28-30 are rejected under 35 U.S.C. 103(a) as being made

obvious by Dodds et al. (US 6,287,254; Issued: Sept. 11, 2001), in view of Luciano et al. (US

6.063,028; Issued May 16, 2000).

Dodds et al. teach a veterinary diagnostic method, system and apparatus of health

profiling of an ánimal subject [Abstract]. More specifically, Dodds et al. teach the following

aspects of the instantly claimed invention:

- Dodds et al. teach the use of phenotypic data [Col. 1, lines 50-65] and genotypic data

  [Col. 2, lines 40-55] and [Col. 11], as in claims 1, 23, 28.

- obtaining genetic data associated with a selected animal; obtaining phenotype health

  assessment data associated with a selected animal (i.e. non-genetic data); combining

the genetic data and the phenotype health assessment data to determine a relationship

between the genetic data and the phenotype health assessment data using a computer

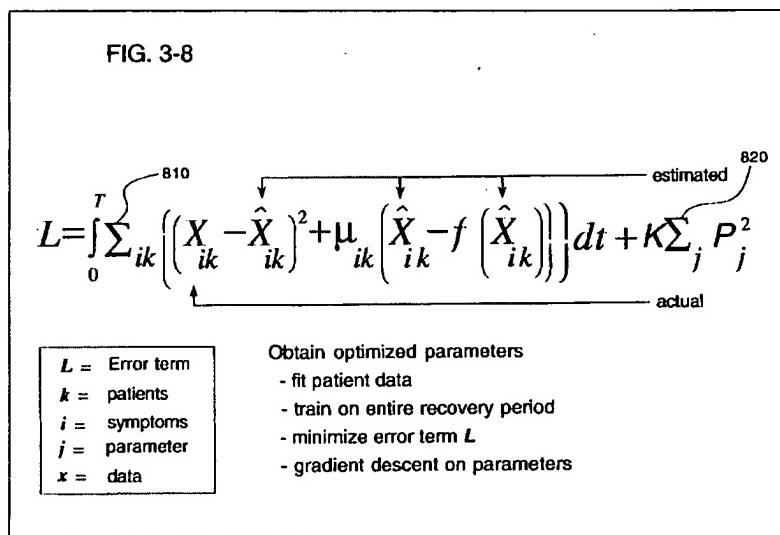program [Ref. Claim 1], as in claims 1 and 9.

- selecting from data relating to temperament of animal, lifespan of animal, or physiologic

  or genetic marker for autoimmune thyroiditis or thyroid dysfunction of the selected

  animal [Ref. Claim 1], which equate to indicators of disease status, as in claim 1.

Dodds et al. also teach a computer system [Fig. 1] for inputting data into a genetic database and

phenotypic database, and other databases, storing the data in these databases, analyzing the

data in a relational sense from the different databases, and retrieving the data from these

databases [Col. 7, ¶ 4], as in claims 20 and 21. Dodds et al. also teach phenotype and genotype

databases wherein data is divided into particular groupings [Col. 21, ¶ 3 and 4], a genetic

marker database [Col. 21, ¶ 6], and an algorithm that relates coefficients and predictability data

(i.e. criteria) from the above data to determine an output [Col. 22, ¶ 3], which the Examiner has

broadly interpreted as a teaching for claim 23.

Dodds et al. do not specifically teach determining weights associated with a model or

optimizing model parameters by minimizing the sum of weighted deviates, where the deviates

are weighted by corresponding weights that reflect genetic data associated with the respective

data sets, as in claims 1, 2, 3, 19, 20, 21, and 28-30. However, Dodds et al. teach the use of

genetic and non-genetic data for building computer driven statistical models for predicting the

occurrence of specific diseases [Col. 7, ¶ 3].

Luciano et al. teach a method predicting disease based upon symptoms (i.e. non-genetic

data) experienced by a patient [Abstract] and [Col. 4, lines 55-65]. A processing unit that

weights the inputted patient data is provided [Col. 4, lines 45-55]. In particular, Luciano shows

fitting data based on determining weights associated with a model and optimization of model

parameters by minimization of sum of weighted squares (i.e. weighted deviates) [See for

example Col. 15, ¶ 2 and ¶4, and Col. 17, lines 45-55], and provides equations for calculating

optimized model parameters based on summations of weighted deviations that incorporate

estimated and actual data [See Fig. 3-8 below]. .

FIG. 3-8

$$L=\int_0^T \Sigma_{ik}\left[\left(X_{ik}-\hat{X}_{ik}\right)^2+\mu_{ik}\left(\hat{X}_{ik}-f\left(\hat{X}_{ik}\right)\right)\right]dt+K\Sigma_j P_j^2$$

L = Error term	Obtain optimized parameters
k = patients	- fit patient data
i = symptoms	- train on entire recovery period
j = parameter	- minimize error term L
x = data	- gradient descent on parameters

Thus it would have been obvious to someone of ordinary skill in the art at the time of the

instant invention to practice the disease risk prediction method taught by Dodds et al. with the

additional model optimization steps taught by Luciano et al., as Dodds et al. suggest continually

updating statistical models to enhance predictive ability [Dodds et al., Col. 7, ¶ 3]. One of

ordinary skill in the art would have been motivated to combine the above teachings in order to

develop an optimized model for improved disease risk prediction [Luciano et al., Col. 5, ¶ 1],

resulting in the practice of the instant claimed invention. One of skill in the art would have had a

reasonable expectation of successfully combining the above teachings both Dodds et al. and

Luciano et al. clearly teach the use of statistical techniques including regression analysis [Dodds

et al. Col. 7, ¶ 3].

Claims 1-15 and 17-30 are rejected under 35 U.S.C. 103(a) as being made obvious by Dodds et al. (US 6,287,254; Issued: Sept. 11, 2001), in view of Tibshirani (STATISTICS IN MEDICINE, 1997, Vol. 16, p.385-395) and Nelson et al. (J Clin Epidemiol, 1998, Vol. 51, No. 3, pp. 199–209).

Dodds et al. teach a veterinary diagnostic method, system, and apparatus for predicting health in animal subjects [Abstract], as set forth above.

Dodds et al. do not specifically teach determining weights associated with a model or optimizing model parameters by minimizing the sum of weighted deviates, where the deviates are weighted by corresponding weights that reflect genetic data associated with the respective data sets, as in claims 1-3, 9-15, 17-22, and 27-30. Dodds et al. also do not specifically teach steps directed to recursive division of data, as in claims 4-7 and 24-26.

Tibshirani teaches a computer-implemented method for determining variables for a Cox proportional-hazard model [Abstract]. More specifically, Tibshirani teaches the following aspects of the instantly claimed invention:

- A plurality of data sets associated with lung and liver cancer studies comprising Karnofsky scores, age, sex, state of disease, cell type, treatment, etc. [p.387] and [p.389], which the Examiner has broadly interpreted as teachings for 'indicator of disease status', and 'non-genetic' data, as in claim 1, 15-18, 28-30.

- A Cox statistical model for calculating risk and dependent on a plurality of parameters comprising time, predictor values, and baselines functions [Section 1, Equations 1 and 2], as in claims 1, 8, 10, 11, 13, 28-30.

- Notation of partial likelihood functions comprising standardized "x" variables that are indexed for association with population members and weighted by N [p.386, ¶ 2], which the Examiner has broadly interpreted as an 'adjustment factor' as in claim 14 and 27.

- An minimization of model parameter via an argmin function (i.e. target function) [p.386, ¶ 1] and an iterative "weighted" least squares algorithm used for minimization of model parameters [p.386, Section 2], as in claim 1.

- Calculating of deviations in data sets using seventeen variables and using full, stepwise, and Lasso models (i.e. which incorporates minimized weighted values as described in Section 2) for data simulations [p.390, Table I] and [p.391, Section 5.2 and Fig. 2], as in claim 1, 20, and 28-30.

- Computation of model parameters using quadratic programming techniques [p.386, Section 2], which is an implicit teaching for computer devices, computer executable instructions, and computer readable mediums, as in claims 1 and 21.

- Calculation of mean squared error and relative risk scores for grouped model parameters and for optimized models (i.e. Lasso), including disease status (x_{17}) [p.389 and Table I], which is an implicit teaching for a difference calculation, as in claim 1.

- Clinical examples wherein data indicative of a plurality of factors is grouped (i.e. by case reference number, sex, age, etc.) according to seventeen variables, wherein groups include values of 0 and 1, and wherein missing values are discarded (i.e. imputing missing data) [p.389, ¶ 1], as in claims 12, 22.

- Comparison of models after simulation for selection of optimum model, wherein one model uses a different number of parameters [Table I], and Lasso model outperforming the rest and selecting appropriate number of coefficients [Table 1] and [p.391, Section 5.1], as in claims 28-30.

Nelson et al. teach the use of recursive partitioning to produce classification trees, wherein subjects are assigned to subsets according to a set of predictor variables [Abstract]. Critical limitations that relate to the instantly claimed invention include: using recursive division of data based on specific criteria for data classification into terminal subsets [Fig. 1], as in claims 24-26. Nelson et al. also teach a splitting criterion (i.e. Gini index) to identifying variable that minimize variance between case (i.e. disease) and control groups (i.e. reference), wherein the Gini index (i.e. weight) is calculated for each group and comprises values between zero and one [p.207 and 208, Appendix A] and [Fig. 1], as in claims 4-7.

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the disease risk prediction method taught by Dodds et al. with the additional use of classification trees based on recursive partitioning as taught by Nelson et al., and the Cox hazard model taught by Tibshirani, as the use of recursive partitioning with disease prediction models is well known [Nelson et al., p.201, Col. 1, ¶ 1] and as Dodds et al. suggest continually updating statistical models to enhance predictive ability [Dodds et al., Col. 7, ¶ 3]. One of ordinary skill in the art would have been motivated to combine the above teachings in order to use optimized model for improved disease risk prediction [Tibshirani, Abstract] and recursive partitioning is well known for improving the accuracy of disease prediction [Nelson et al., p.201, Col. 1, ¶ 1], resulting in the practice of the instant claimed invention. One of skill in the art would have had a reasonable expectation of successfully combining the above teachings as Dodds et al. clearly teaches the use of statistical techniques including regression analysis [Dodds et al. Col. 7, ¶ 3] and as Tibshirani and Nelson et al. also teach methods of regression analysis [p.204, Col. 1, ¶ 2].

Response to Arguments

Applicant's arguments, filed 9/28/2007, that appear to assert that Dodds and Luciano fail to teach a statistical model for calculating disease risk as a function of non-genetic data have been fully considered but are not persuasive. Dodds shows using a computer program (i.e. model) to determine a relationship between genetic data and phenotype health assessment data; select data from i) the temperament of the selected animal (i.e. non-genetic data), ii) data relating to the lifespan of the selected animal (i.e. non-genetic data), or iii) a physiologic or genetic marker for autoimmune thyroid dysfunction of the selected animal (i.e. genetic data); and analyzing the selection of one of the above data types for calculation of health, disease or disorder probabilities (i.e. risk) to enhance the quality of life of a selected animal [See Ref. claim 1]. Therefore, Dodds at a minimum suggests the use of a computer model that calculates disease risk as a function of non-genetic data sets. Luciano was relied upon as a teaching for optimization of model parameters using weighted deviates.

Applicant's arguments, filed 9/28/2007, that Dodds and Luciano fail to teach "parameters that are optimized using weights which are dependent on the genetic data" have been fully considered but are not persuasive. Claim 1 requires optimizing parameters of the candidate model by fitting, wherein said fitting comprises: calculating for each of said sets, a deviate of a predicted risk from an indicator of disease status for that set, said predicted risk predicted using said candidate model and non-genetic data in that set; calculating a sum of weighted deviates for all of said sets, wherein each deviate is weighted in said sum by the weight associated with that set for which said each deviate has been calculated; and minimizing said sum of weighted deviates to obtain optimized parameters. Therefore the features upon which applicant relies (i.e., parameters that are optimized using weights which are dependent on the genetic data) are

not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, Luciano [Col. 15, ¶ 2] and [[Col. 17, lines 45-55] shows the optimization of model parameters that yield the best fit to the data through minimization parameters including patient data. This rejection is maintained.

Applicant's arguments, filed 9/28/2007, that Tibshiriani and Nelson et al. do not teach "optimizing model parameters by minimizing the sum of weighted deviates, where the deviates are weighted by corresponding weights that reflect genetic data associated with the respective data sets" have been fully considered but are not persuasive. Tibshiriani and Nelson et al. were not relied upon as a teaching for this limitation. Tibshirani was relied upon as teaching for determining variables for a Cox proportional-hazard model [Abstract]. Nelson et al. was relied upon as teaching for recursive partitioning to produce classification trees, wherein subjects are assigned to subsets according to a set of predictor variables [Abstract]. Contrary to applicant's position, Dodds at a minimum suggests the use of a computer model that calculates disease risk as a function of non-genetic data sets, as explained above. Therefore all elements of the claimed invention are disclosed by the cited references. Because there is no element or part of applicant's claimed subject matter which is not suggested or specifically disclosed, this rejection is maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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